# United States Patent [19]

**Rubinstein et al.**

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[54] **PROCESS FOR THE CROSS-LINKING OF PROTEINS**


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[58] **Field of Search** ..... 195/63, 68, DIG.11; 260/112 R, 117, 122



[56] **References Cited**

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[57] **ABSTRACT**

The invention relates to a process for the cross-linking of proteins wherein the proteins to be cross-linked are reacted with a cross-linking agent selected from the group consisting of:

(a) water soluble poly(ethylene oxide) derivatives of the general formula I

$$(Z)_m—Y—(CH_2CH_2O)_nCH_2CH_2—Y—(Z)_m \quad (I)$$

wherein both n and m are at least 1; Y is a covalent bond or is an —R— or —RO— radical in which the oxygen is bound to the poly(ethylene oxide) and R is selected from the group consisting of methylene, ethylene, propylene, o—, m— and p-phenylene, o—, m— and p-phenylene carbamate optionally substituted by one or more alkyl, aryl, halo, nitro, oxo, carboxy, hydroxy, thio, sulfonate and phosphate groups; and Z is a reactive group selected from the groups consisting of haloisocyanato-, isothiocyanato-, tosylate, acyl halides, acyl azides, aryl diazonium salts, acyl imidoester salts, activated esters of acyl residues and 2,4-dichlorotriazines; and

(b) activated esters of di- and poly-carboxylic acids wherein the acids and the alcohol moieties thereof are water soluble.


**31 Claims, No Drawings**